

1. (Currently amended) A method of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue, wherein the tissue is at least one of in vivo or an internal tissue; and

compensating for macroscopic motion to isolate the microscopic motion.

2. (Previously presented) The method of claim 1, wherein the microscopic motion is Brownian motion.

3. (Previously presented) The method of claim 1, wherein the microscopic motion is motion of cells or cellular organelles.

Claims 4-6 (Cancelled).

7. (Previously presented) The method of claim 1, wherein the illuminating step comprises providing an invasive device coupled to a light source, passing the device into a patient, placing the device in proximity to the tissue, and shining coherent or partially coherent light from the light source onto the tissue.

8. (Previously presented) The method of claim 7, wherein the invasive device is selected from the group consisting of a catheter, an endoscope, and a laparoscope.

9. (Previously presented) The method of claim 7, wherein the placing step includes placing the device in direct contact with the tissue.

10. (Previously presented) The method of claim 1, wherein the coherent light comprises laser light.

Claim 11 (Cancelled).

12. (Previously presented) The method of claim 1, wherein a detector is located farther than one wavelength of light from the tissue and detects far field speckle.

13. (Previously presented) The method of claim 1, wherein a detector is located within one wavelength of light from the tissue and detects near field speckle.

14. (Previously presented) The method of claim 1, wherein the analyzing step comprises comparing each of the series of speckle patterns to a series of reference speckle patterns, and quantifying the temporal correlation differences between the speckle patterns and the reference patterns.

15. (Previously presented) The method of claim 14, wherein the analyzing step comprises digitizing each of the speckle patterns, and the quantifying step comprises evaluating a cross-correlation between the speckle patterns and the reference patterns.

16. (Previously presented) The method of claim 14, wherein the analyzing step comprises digitizing each of the speckle patterns, and the quantifying step comprises evaluating a maximum cross-correlation between the speckle patterns and the reference patterns.
17. (Previously presented) The method of claim 15, wherein the analyzing step further comprises determining a decorrelation rate for the speckle patterns.
18. (Previously presented) The method of claim 1, wherein the analyzing step further comprises analyzing spatial characteristics of the speckle pattern to deduce structural characteristics of the tissue.
19. (Previously presented) The method of claim 1, wherein the analyzing step further comprises analyzing spatial characteristics of the speckle pattern to deduce biomechanical characteristics of the tissue.
20. (Previously presented) The method of claim 18, wherein the illuminating step comprises illuminating multiple locations of the tissue in succession, the receiving step comprises forming a separate series of speckle patterns for each respective section of the tissue, and the analyzing step comprises analyzing each separate series of speckle patterns and comparing the separate series to deduce structural differences between the respective locations of the tissue.

21. (Currently amended) The method of claim [4]1, wherein the compensating for the macroscopic motion comprises performing the receiving step during a diastole of a heartbeat.

22. (Currently amended) The method of claim [4]1, wherein the macroscopic motion comprises a patient motion.

23. (Currently amended) The method of claim [4]1, wherein the macroscopic motion is peristalsis.

24. (Currently amended) The method of claim [4]1, wherein the receiving step comprises gathering reflected light at a light receptor and transmitting the gathered light to a detector, and wherein compensating for macroscopic motion includes coupling the receptor to the tissue.

25. (Currently amended) The method of claim [4]1, wherein the compensating for the macroscopic motion includes excluding changes in the speckle patterns caused by non-random motion during the analysis step.

26. (Previously presented) A method of analyzing tissue, the method comprising:  
illuminating a tissue with coherent or partially coherent light;  
receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by a microscopic motion of objects within the tissue; and  
compensating for a macroscopic motion to isolate the microscopic motion, wherein the macroscopic motion results from a motion or the deformation of the tissue.

27. (Previously presented) The method of claim 1, wherein the tissue comprises an atherosclerotic plaque.

Claims 28–38 (Cancelled).

39. (Currently amended) A method of analyzing a tissue structure, the method comprising:

illuminating the tissue structure with coherent or partially coherent light;

receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue; and

assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure,

wherein the spatial characteristics are analyzed by assessing a thickness of the tissue structure, and

wherein the tissue structure thickness is assessed by:

(i) measuring the decorrelation time constant  $r$  as a function of  $r = (x_0^2 + y_0^2)^{1/2}$ ,

(ii) measuring optical properties of the tissue structure, and

(iii) comparing the measured optical properties and  $\tau(r)$  to a mathematical simulation that models light remittance as a function of tissue structure thickness.

Claims 40 and 41 (Cancelled).

42. (Currently amended) The method of claim [41]39, wherein the optical properties are measured by computing first and second order statistics of a speckle probability distribution function or by using diffuse reflectance spectrophotometry.

43. (Currently amended) The method of claim [41]39, wherein the mathematical simulation is a Monte Carlo simulation or diffusion theory simulation.

Claims 44-61 (Cancelled).

62. (Currently amended) A ~~The method of claim 27, further comprising of analyzing tissue which comprises an atherosclerotic plaque, the method comprising:~~

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue, wherein the tissue is at least one of in vivo or an internal tissue; and

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion.

63. (Previously presented) The method of claim 62, further comprising analyzing spatial characteristics of the speckle pattern data to deduce structural characteristics of the plaque.

64. (Previously presented) The method of claim 63, wherein analyzing comprises assessing the thickness of the fibrous cap.

65. (Previously presented) The method of claim 64, wherein cap thickness is assessed by

- (i) measuring the decorrelation time constant  $\tau$  as a function of  $r = (x_0^2 + y_0^2)^{1/2}$ ;
- (ii) measuring optical properties of the cap; and
- (iii) comparing the measured optical properties and  $\tau(r)$  to a mathematical simulation that models light remittance as a function of cap layer thickness.

66. (Previously presented) The method of claim 65, wherein the optical properties are measured by computing first and second order statistics of a speckle probability distribution function or by using diffuse reflectance spectrophotometry.

67. (Previously presented) The method of claim 65, wherein the mathematical simulation is a Monte Carlo simulation or diffusion theory simulation.

68. (Previously presented) The method of claim 64, wherein a plaque is considered vulnerable to rupture if the thickness of the fibrous cap is less than about 60 microns.

69. (Previously presented) The method of claim 63, wherein analyzing comprises assessing the viscosity of the lipid pool.

70. (Previously presented) A method of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light, wherein the tissue comprises an atherosclerotic plaque;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion, wherein the plaque is considered vulnerable to rupture if the viscosity of the lipid pool has a time constant of less than about 200 milliseconds.

71. (Previously presented) A method of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light, wherein the tissue comprises an atherosclerotic plaque;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion, wherein the plaque is considered likely to rupture if the viscosity of the lipid pool has a time constant of less than about 100 milliseconds.

72. (Previously presented) The method of claim 39, wherein the tissue structure comprises an atherosclerotic plaque.

73. (Currently amended) A The method of claim 40 of analyzing a tissue structure of which comprises an atherosclerotic plaque, the method comprising:

illuminating the tissue structure with coherent or partially coherent light;  
receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue; and

assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure, wherein tissue structure thickness is assessed by analyzing variation of  $\tau$  as a function of distance from a center of the speckle pattern as a function of  $(x_o^2 + y_o^2)^{1/2}$ .

74. (Previously presented) The method of claim 64, wherein thickness of the fibrous cap is assessed by analyzing variation of  $\tau$  as a function of distance from a center of the speckle pattern as a function of  $(x_o^2 + y_o^2)^{1/2}$ .

75. (Currently amended) A The method of claim 1 analyzing tissue, comprising:  
illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes  
caused by microscopic motion of objects within the tissue, wherein the tissue is at least one of in  
vivo or an internal tissue, wherein the analyzing step comprises measuring biomechanical properties  
of the tissue in three dimensions.

76. (Currently amended) A The method of claim 39 analyzing a tissue structure, comprising:

illuminating the tissue structure with coherent or partially coherent light;  
receiving light reflected from the tissue structure at a detector and forming a series of speckle  
patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion  
within the tissue structure or adjacent tissue; and

assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to  
deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure  
is at least one of in vivo or an internal tissue structure, wherein the analysis of the special  
characteristics includes a measurement of analyzing comprises measuring biomechanical properties  
of the tissue in three dimensions.

77. (Currently amended) A The method of claim 1 analyzing tissue, comprising:

illuminating a tissue with coherent or partially coherent light;  
receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue, wherein the tissue is at least one of in vivo or an internal tissue, wherein the analyzing step comprises determining a collagen content of the tissue.

78. (Currently amended) A ~~The~~ method of ~~claim 1~~ analyzing tissue, comprising:

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

and

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue, wherein the tissue is at least one of in vivo or an internal tissue, wherein the analyzing step comprises determining a viscosity of a lipid pool within the tissue.

79. (Currently amended) A ~~The~~ method of ~~claim 39~~ analyzing a tissue structure, comprising:

illuminating the tissue structure with coherent or partially coherent light;

receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue; and

assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure, wherein the analysis of the special

characteristics includes a determination of analyzing comprises determining a collagen content of the tissue.

80. (Currently amended) A The method of claim 39 analyzing a tissue structure, comprising:  
illuminating the tissue structure with coherent or partially coherent light;  
receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;  
gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue; and  
assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure, wherein the analysis of the special characteristics includes a determination of analyzing comprises determining a viscosity of a lipid pool within the tissue.

81. (Previously presented) The method of claim 62, wherein the microscopic motion is Brownian motion or cellular motion.

82. (Previously presented) A method of analyzing tissue, the method comprising:  
illuminating a tissue with coherent or partially coherent light;  
receiving light reflected from the tissue at a detector and forming series of speckle patterns;  
analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue; and

at least partially replacing blood provided in or adjacent to the tissue with at least partially transparent solution.

83. (Previously presented) A method of analyzing tissue, the method comprising:

illuminating a tissue with coherent or partially coherent light;

receiving light reflected from the tissue at a detector and forming series of speckle patterns;

analyzing changes in the speckle patterns at time intervals sufficient to measure changes caused by microscopic motion of objects within the tissue;

compensating for a macroscopic motion to isolate the microscopic motion, wherein the macroscopic motion results from a motion or the deformation of the tissue; and

at least partially replacing blood provided in or adjacent to the tissue with at least partially transparent solution.

84. (Currently amended) A The method of claim 39 analyzing a tissue structure, comprising:

illuminating the tissue structure with coherent or partially coherent light;

receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue;

assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure; and

compensating for macroscopic motion to isolate the microscopic motion.

85. (Currently amended) A ~~The~~ method of claim 39 analyzing a tissue structure, comprising:

illuminating the tissue structure with coherent or partially coherent light;

receiving light reflected from the tissue structure at a detector and forming a series of speckle patterns;

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within the tissue structure or adjacent tissue;

assessing the tissue structure by analyzing spatial characteristics of the speckle pattern data to deduce structural or biomechanical characteristics of the tissue structure, wherein the tissue structure is at least one of in vivo or an internal tissue structure, wherein the tissue structure comprises an atherosclerotic plaque; and further comprising

gathering speckle pattern data at time intervals sufficient to measure microscopic motion within a lipid pool within the atherosclerotic plaque; and assessing the atherosclerotic plaque's vulnerability to rupture from the amount of microscopic motion.